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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,449	06/28/2002	Istvan Szelenyi	033285-010	9422

21839 7590 04/30/2007
BUCHANAN, INGERSOLL & ROONEY PC
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
KANTAMNENI, SHOBHA	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
04/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/089,449	SZELENYI ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *1-4, 7-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 02/13/2007, wherein claim 1 has been amended.

Applicant's arguments have been fully considered, but not found persuasive, and the rejection of claims 1-4, and 8 under 35 U.S.C. 103(a) as being unpatentable over Keller et al. (WO 9834595, English equivalent to US 6461591, PTO-892 of record), in view of Douglas (EP 0416950, PTO-892) is MAINTAINED. See under response to arguments.

Applicant's arguments have been fully considered, but not found persuasive, and the rejection of claim 7 under 35 U.S.C. 103(a) as being unpatentable over Keller et al. in view of Doi, Koji (WO 9831343 of record) and Bjerkec (of record) and van der Molen is MAINTAINED. See under response to arguments.

Currently, Claims 1-4, and 7-8 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keller et al. (WO 9834595, English equivalent to US 6461591, PTO-892 of record), in view of Douglas (EP 0416950, PTO-892).

Keller et al. discloses a inhalable medicinal aerosol composition or formulation comprising an effective amount of a pharmaceutically active compound selected from the group consisting of beta-mimetics such as salbutamol, reproterol, salmeterol, or formoterol, and an effective amount of a corticoids such as loteprednol. See US 6461591, claims 8, 17, 3-4; column 10, lines 58-62.

Keller et al. does not specifically teach the composition therein in powdered form.

Keller et al. does not expressly disclose a process for the preparation of the inhalable medicinal composition therein in the powdered form.

Douglas teaches pharmaceutical compositions comprising effective amounts of beta-mimetics, salmeterol, and corticosteroid, beclomethasone dipropionate as a combined preparation for simultaneous, sequential or separate administration by inhalation in the treatment of asthma, and other respiratory disorders. See abstract; page 2, lines 1-35. It is also taught that the compositions therein can be administered by inhalation or insufflation, and the inhalation compositions can take the form of a dry powder composition, obtained by mixing the active ingredients and a suitable carries such as lactose. See page 3, lines 18-20; page 5, EXAMPLE 5-EXAMPLE 8. The process for making dry powder formulation, which can be administered by inhalation is also taught. See page 6, lines 37-42. It is also taught that the inhalable compositions therein, provide effective treatment and therapy for asthmatics. See page 2, lines 35-41.

It would have been obvious to a person of ordinary skill in the art at the time of invention to prepare the formulation for administration by inhalation route containing

beta-mimetics such as salbutamol, reproterol, salmeterol, or formoterol, and corticoid, loteprednol taught by Keller et al. in the form of dry powder.

One of ordinary skill in the art at the time of invention would have reasonably expected to obtain an inhalable composition in the powered form by mixing well known beta-mimetics such as formoterol, salmeterol, reproterol, and corticosteriod, loteprednol because Douglas teaches process for making formulations containing beta-mimetics and corticosteroids, in the powdered form for inhalation.

Moreover, note that it is well settled that "intended use" of a composition or product, e.g., "in the treatment of ashma brochiale", will not further limit claims drawn to a composition or product, so long as the prior art discloses the same composition comprising the same ingredients in an effective amount as the instantly claimed. See, e.g., *Ex parte Masham*, 2 USPQ2d 1647 (1987) and *In re Hack* 114, USPQ 161.

Response to Applicant's Arguments

Applicant argues that " Keller does not disclose the claimed powdered formulations comprising: (i) loteprednol or loteprednol etabonate and (ii) at least one β2 adrenoreceptor agonists. Applicants note that pressure-liquefied aerosol formulations are different from powdered formulations recited in claims 1-4." This argument has been considered, but not found persuasive because applicant is arguing against a single reference when the rejection was based on combination of references.

Applicant argues that "Because Palmer Douglas does not disclose loteprednol or loteprednol etabonate, Palmer Douglas cannot be relied on to demonstrate point (3)-the

teaching of all claim limitations, or point (1)-the suggestion/motivation to modify or combine the reference teachings." This argument has been considered, but not found persuasive. Keller et al. discloses a inhalable medicinal aerosol composition or formulation comprising an effective amount of a pharmaceutically active compound selected from the group consisting of beta-mimetics such as salbutamol, reproterol, salmeterol, or formoterol, and an effective amount of a corticoids such as loteprednol, beclomethasone dipropionate, and Palmer Douglas teaches formulations comprising beta-mimetics, salmeterol, and corticosteroids such as beclomethasone dipropionate in the powdered form for inhalation. One of ordinary skill in the art at the time of invention would have been motivated to employ beta-mimetics such as reproterol, salmeterol, or formoterol and corticoids such as loteprednol, beclomethasone dipropionate taught by Keller et al. in powdered form with reasonably expectation of obtaining an inhalable composition because according to Douglas process for making formulations containing beta-mimetics , and corticosteroids, in the powdered form for inhalation is well known.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Keller et al. in view of Doi, Koji (WO 9831343 of record) and Bjerkec (of record) and van der Molen (of record), the rejection of record.

The same disclosure of Keller et al. has been discussed in the 103(a) rejection set forth above.

Keller et al. does not expressly disclose the employment of the inhalable medicinal aerosol composition comprising the combination as instantly claimed in a method for the treatment of ashma bronchiale for simultaneous, sequential or separate administration.

Doi discloses that loteprednol etabonate is known to be useful in a pharmaceutical composition and a method of treating inflammatory conditions or allergy since loteprednol etabonate has excellent anti inflammatory and antiallergic activities and is value as a drug in an ointment or a liquid form, and loteprednol etabonate is formulated into a long-term stable liquid suspension for nasal administration (see abstract page 1, lst and 2nd paragraphs, Examples at page 7-11 claims 1-5).

Ashma bronchiale is a known inflammatory condition or allergy.

According to Bjermer, long-acting ß2 agonists, for example, salmeterol and formoterol, are bronchospasmolytics, are used as inhalations in asthma treatment. These long-acting ß2 agonists should always be given in combination with corticosteroids. Short-acting ß2 agonists, for example, salbutamol, may be given additionally (see abstract, page 587 'Introduction'; page 589, right-hand column, paragraph 4; page 590 'Conclusion'). The corticosteroids indicated include

beclomethasone dipropionate, budesonide and fluticasone propionate (see page 588, left-hand column, lïnes 1-2; page 589, right-hand column, line 19).

The clinical study described in van der Molen shows that the symptoms of asthma patients are improved on inhalation of the long-acting ß2 agonist, formoterol in as addition to inhaled corticosteroids (see abstract; page 536 'Subjects'; page 538 'Discussion'). Van der Molen does not specify the corticosteroids used.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ loteprednol etabonate in combination with reproterol, salmeterol, or formoterol in a method for the treatment of allergies and/or airway disorders such as ashma brochiale for simultaneous, sequential or separate administration.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ loteprednol etabonate in combination with reproterol, salmeterol, or formoterol in a method for the treatment of allergies and/or airway disorders such as ashma brochiale for simultaneous, sequential or separate administration, since both loteprednol etabonate, and reproterol, salmeterol, or formoterol, are known to be useful in a pharmaceutical composition and a method for the treatment of allergies and/or airway disorders such as asthma based on the prior art.

Therefore, one of ordinary skill in the art would have reasonably expected that combining loteprednol etabonate and reproterol, salmeterol, or formoterol both known useful for the same purpose, i.e., treating allergies and/or airway disorders such as

asthma, would improve the therapeutic effects for treating the same diseases, and/or would produce additive therapeutic effects in treating the same.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Moreover, the teachings of Bjermer and van der Molen have further clearly provided the motivation for the instant combination, because long-acting ß2 agonists, should always be given in combination with corticosteroids according to Bjermer. The clinical study described in van der Molen shows that the symptoms of asthma patients are improved on inhalation of the long-acting ß2 agonist, formoterol in addition to inhaled corticosteroids. It is noted that loteorednol etabonate is the particular corticosteroid. Further, the process for preparation of a pharmaceutical composition herein is considered well within conventional skills in pharmaceutical science.

Thus the claimed invention as a whole is seen prima facie obvious over the combined teachings of the prior art.

Response to Arguments

Applicant's argument that "none of the cited references suggest the combination of the elements of the method recited in Claim 7" is not found persuasive because Keller as discussed above discloses medicinal or pharmaceutical aerosol compositions comprising beta-mimetics and corticoids. Corticoids such as loteprednol,

beclomethasone, and beta-mimetics such as salbutamol, reproterol, salmeterol, formoterol are disclosed. Bjermer, and Van der Molen teach that ß2 agonists for example salmeterol, formoterol are used as inhalations in inflammatory conditions such as asthma treatment, and should be given in combination with corticosteroids. Doi discloses that loteprednol etabonate is known in the method of treating inflammatory conditions or allergy (asthma bronchiale is a Respiratory disorder characterized by wheezing; usually of allergic origin). One of ordinary skill in the art at the time of invention would have been motivated to combine corticosteroid loteprednol with beta-mimetics with reasonable expectation of treating inflammatory condition such as asthma because 1) according to Bjermer, and Van der, ß2 agonists for example salmeterol, formoterol are used as inhalations in inflammatory conditions such as asthma treatment, and should be given in combination with corticosteroids, and 2) loteprednol is a corticosteroid.

Applicant argues that "if Doi does not describe the use of loteprednol etabonate-containing nasal drips for the treatment of "airway disorders such as asthma bronchiale," then how is the holding of *In re Kirkhoven* relevant here, when the purpose of Doi (anti-allergic agent) is not the same purpose as the method of claim 7 (treatment of asthma bronchiale)?" This argument has been considered, but not found persuasive because Doi teaches that loteprednol etabonate is formulated into a long-term stable liquid suspension for nasal administration and is employed in the method of treating inflammatory conditions or allergy (asthma bronchiale is a Respiratory disorder characterized by wheezing; usually of allergic origin). Therefore, one of ordinary skill in

the art would have reasonably expected that combining loteprednol etabonate and reproterol, salmeterol, or formoterol both known useful for the same purpose, i.e., treating inflammatory conditions or allergies and/or airway disorders such as asthma, would improve the therapeutic effects for treating the same diseases. It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. As shown by recited teachings of Doi, Bjermer, and Van der, the instant claims contain two compositions used for the same purpose i.e treating inflammatory conditions or allergies and/or airway disorders such as asthma (asthma bronchiale is a Respiratory disorder characterized by wheezing; usually of allergic origin) such as asthma treatment. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Applicant's arguments with regards to unexpected results, and testing data herein have been fully considered but are not persuasive as to the nonobviousness and/or unexpected results of the claimed invention over the prior art. The results on the tests of the employment of salbutamol and loteprednol; formoterol and loteprednol would be expected according to the teachings of Bjerkec and van der Molen, because long-acting ß2 agonists, should always be given in combination with corticosteroids according to Bjerkec. The clinical study described in van der Molen shows that the symptoms of asthma patients are improved on inhalation of the long-acting ß2 agonist, formoterol in addition to inhaled corticosteroids. It is noted that loteprednol etabonate is

the particular corticosteroid. Note that expected beneficial results are evidence of obviousness. See MPEP § 716.02(c). Therefore, the evidence presented in specification herein is not seen to be clear and convincing in support the nonobviousness of the instant claimed invention over the prior art

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

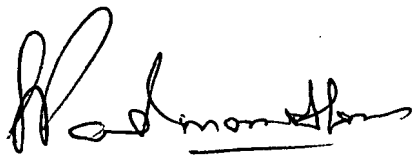
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period, will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Tuesday, Thursday-Friday, 8am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shobha Kantamneni, Ph.D
Patent Examiner
Art Unit : 1617



SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER